REMARKS

The Office Action of December 24, 2003, has been received and reviewed. All claim amendments are made without prejudice or disclaimer. Claims 28 and 48 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking sufficient written description and enablement commensurate with the scope of the claims. Reconsideration is respectfully requested.

Support for claim amendments:

Support for claims 49 to 58 can be found throughout the specification, for example, at paragraphs 12, 23, 28, 75-78, and Table 2.

Written Description rejection:

Claims 28 and 48 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description. The Office asserts that there is no clear depiction of what structures or properties of the Ad5 protein fragments are required for generation of the recited recombinant adenovirus fiber proteins to produce tropism for mesenchymal stem cells (page 3 of the Office Action). The applicants respectfully disagree.

The Office acknowledges that the specification teaches that fiber proteins from adenovirus serotypes such as 16, 35, 40-S and 51 (*Id.*) provide tropism for mesenchymal stem cells. The specification also teaches the trimeric structure of the fiber protein and that the tail region, for example, the conserved FNPVYP sequence, is involved in anchoring the fiber to the penton base (*see*, for example, paragraph [0040]). The specification also teaches that the knob region is responsible for initial interactions with the cellular adenovirus receptor (*Id.*).

A "patent specification is not intended nor required to be a production specification" (MPEP § 608.01(h)). In the present case, when combined with the knowledge of a person of ordinary skill in the art, the instant specification provides a written description of the correlation between the structure of a fragment of a fiber protein and tropism. For example, Krasnykh *et al.* (copy provided herewith), which is cited in paragraph [0040], discloses the generation of a recombinant fiber protein wherein the knob domain from Ad3 replaces the knob domain of Ad5.

Krasnykh *et al.* demonstrates that a person of ordinary skill in the art is able to produce a functional chimeric fiber protein using the knob domain of a second subgroup.

Further, the same reasoning applies to the structures and properties of the Ad5 protein used to generate a recombinant adenovirus vector, which, for example, may be the tail region. In addition, a person of ordinary skill in the art would also recognize that the length and source of the stem region may vary without departing from the invention.

Using the applicants' disclosure of the tropism for mesenchymal stem cells, the disclosure of the general structure of fiber proteins and their interactions with cellular receptors, coupled with the information known in the art, a person of skill in the art would recognize that the inventors were in possession of the genus claimed in claims 28 and 48 at the time of filing. Particularly, in view of express statements in the specification, such as "a fiber protein comprising at least a tissue tropism determining part of a subgroup B adenovirus fiber protein, in particular of a serotype 11, 16, 35 and/or 51" (paragraph 13 of the specification).

With regard to claims 49-53, 56 and 57, the Office has acknowledged that the specification provides adequate written description of the replacement of Ad5's fiber protein with a fiber protein of an adenoviral serotype selected from the group consisting of 16, 35, 40-S and 51 (page 3 of the Office Action). In addition, the specification teaches that Ad5 is a representative of subgroup C, for example, at paragraphs 12 and 23. Thus, the applicants submit that claims 49-53, 56 and 57 have sufficient written description.

Enablement rejection:

Claims 28 and 48 also stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement commensurate with the scope of the claims. The Office asserts that the invention requires a complex combination of molecular cloning in combination with viral and cell culture techniques (page 4 of the Office Action). The applicants note that molecular cloning has become routine in the art and that viral and cell culture techniques are also well known in the art. Thus, these aspects of the invention cannot amount to undue experimentation. Moreover, the demonstration in cell culture that the recombinant adenoviral vector infects mesenchymal

stem cells provides the person of skill in the art with the tools necessary to administer the recombinant adenoviral vector *in vivo*. For example, the vector may be injected into bone marrow so as to provide an enriched concentration of viral particles in contact with mesenchymal stem cells. Thus, the specification should enable a person of ordinary skill in the art to administer the recombinant adenoviral vector *in vivo*.

Nevertheless, to expedite prosecution, claims 50 and 54-61 now recite administering the recombinant adenoviral vector *in vitro*. The recitation of administering the recombinant adenoviral vector *in vitro* is believed to moot the rejection with respect to these claims.

Conclusion

In the event questions remain after consideration of these remarks and amendments, the Office is kindly requested to contact applicants' attorney at the number given below.

Respectfully submitted,

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